MARKED UP COPY OF AMENDMENTS

In the Specification

On page 15, line 25, please replace "Applied BioSystems" with "APPLIED BIOSYSTEMS®".

On page 23, line 18, please replace "Marcol" with "MARCOL®"

On page 23, line 18, please replace "Montanide" with "MONTANIDE®"

In the Claims

Please amend the following claims by deleting the words in brackets and inserting the underlined words.

1. (Amended) A method of preventing a pathoangiogenic condition in a mammal comprising: administering to said mammal an amount of one or more [GBS] Group B β-hemolytic *Streptococci* toxin receptors or immunogenic fragments thereof effective to induce or maintain an immune response to at least one of the [GBS] Group B β-hemolytic *Streptococci* toxin receptors,

whereby the development of said pathoangiogenic condition in the mammal is prevented,

wherein the pathangiogenic condition comprises cancer,

and wherein the [GBS] Group B β-hemolytic *Streptococci* toxin receptor comprises HP59 or SP55.

3. (Cancel) The method of claim 1 or 2, wherein the pathangiogenic condition is selected from the group consisting of cancer, scarring during wound healing, gliosis during repair of nerve injury, chronic wounds, keloids, reperfusion injury, rheumatoid arthritis, atherosclerosis, osteoarthritis, and psoriasis.

4. (Amended) The method of claim 1 [or 2], wherein at least one of the [GBS] Group B β-hemolytic *Streptococci* toxin [receptor] receptors has substantial identity to SEQ ID NO: 2.

5. (Amended) The method of Claim 4, wherein at least one of the [GBS] Group B β-hemolytic *Streptococci* toxin [receptor] receptors is identical to SEQ ID NO: 2, or is SEQ ID NO: 2 with at least one conservative amino acid substitution.

6. (Amended) The method of claim 1 [or 2], wherein at least one immunogenic fragment has substantial identity to a portion of SEQ ID NO: 2.

8. (Amended) The method of claim 1 [or 2], wherein at least one of the [GBS] Group B β-hemolytic *Streptococci* toxin [receptor] receptors has substantial identity to SEQ ID NO: 4.

9. (Amended) The method of claim 8, wherein at least one other [GBS] Group B β-hemolytic *Streptococci* toxin [receptor] receptors has substantial identity to SEQ ID NO: 2.

10. (Amended) The method of claim 8, wherein at least one other [GBS] Group B β-hemolytic *Streptococci* toxin receptor is identical to SEQ ID NO: 4, or is SEQ ID NO: 4 with at least one conservative amino acid substitution.

11. (Amended) The method of claim 1 [or 2], wherein at least one immunogenic fragment has substantial identity to SEQ ID NO: 4.

12. (Amended) The method of claim 11, [wherein each of the two or more] the immunogenic fragment has substantial identity to a portion of SEQ ID NO: 4.

14. (Amended) The method of claim 12, wherein at least one immunogenic fragment has substantial identity to a peptide encoded by amino acid residues 9-35 of SEQ ID NO: 4, a peptide encoded by amino acid residues 8-22 of SEQ ID NO: 4, or a peptide encoded by amino acid residues 71-84 of SEQ ID NO: 4.[p55a, p56a, p57a.]

15. (Amended) The method of claim 1 [or 2], wherein the normal tissue of the mammal does not contain the [GBS] Group B β-hemolytic *Streptococci* toxin receptor.

16. (Amended) The method of claim 1 [or 2], wherein the administering is via a method selected from the group consisting of oral ingestion, nasal inhalation, subcutaneous injection, intravenous injection, intramuscular injection, intraperitoneal injection [or] and rectal injection.

29. (Amended) A composition comprising one or more [GBS] Group B β-hemolytic *Streptococci* toxin receptors or immunogenic fragments thereof, wherein the GBS toxin receptor comprises HP59 and SP55.

30. (Amended) The composition of claim 30, wherein one or more [GBS] Group B β-hemolytic *Streptococci* toxin receptors or immunogenic fragments thereof are in an amount effective for protecting against or attenuating a pathoangiogenic condition in a mammal, wherein the pathoangiogenic condition comprises cancer.

32. (Amended) The composition of claim 30, wherein at least one of the [GBS] Group B β-hemolytic *Streptococci* toxin receptors or fragments thereof is isolated.

35. (Amended) The composition of claim 32, wherein one of the isolated [GBS] Group B β-hemolytic *Streptococci* toxin receptors or fragments thereof is conjugated or linked to a protein carrier.

37. (Amended) The composition of claim 30, wherein at least one of the [GBS] Group B β-hemolytic *Streptococci* toxin receptors or fragments thereof is glycosylated.

38. (Amended) The composition of claim 30, wherein at least one of the [GBS] Group B β-hemolytic *Streptococci* toxin receptors or fragments thereof is recombinant or synthetic.

39. (Cancel) The composition of claim 30, wherein the pathoangiogenic condition is selected from the group consisting of cancer, scarring during wound healing, gliosis during repair of nerve injury, chronic wounds, keloids, reperfusion injury, rheumatoid arthritis, atherosclerosis, osteoarthritis, and psoriasis.

40. (Amended) The composition of claim 30, wherein at least one other [GBS] Group B β-hemolytic *Streptococci* toxin receptor has substantial identity to SEQ ID NO: 2.

41. (Amended) The composition of claim 40, wherein at least one of the [GBS] Group B β-hemolytic *Streptococci* toxin receptor is identical to SEQ ID NO: 2, or is SEQ ID NO: 2 with at least one conservative amino acid substitution.

42. (Amended) The composition of claim 40, wherein at least one other [GBS] Group B β-hemolytic *Streptococci* toxin receptor has substantial identity to SEQ ID NO: 4.

44. (Amended) The composition of claim 30, wherein at least one immunogenic fragment has substantial identity to a peptide encoded by amino acid residues 49-63 of SEQ ID NO:1, a peptide encoded by amino acid residues 112-125 of SEQ ID NO:1, a peptide encoded by amino acid residues 8-28 of SEQ ID NO:1, or a peptide encoded by amino acid residues 49-76 of SEQ ID NO:1 [Hab1, Hab2, Hab3 or Hab 4].

45. (Amended) The composition of claim 30, wherein at least one [GBS] Group B β-hemolytic *Streptococci* toxin receptor has substantial identity to SEQ ID NO: 4.

46. (Amended) The composition of claim 45, wherein at least one other [GBS] Group B β-hemolytic *Streptococci* toxin receptor is identical to SEQ ID NO: 4, or is SEQ ID NO: 4 with at least one conservative amino acid substitution.

48. (Amended) The composition of claim 47, wherein at least one immunogenic fragment has substantial identity to a peptide encoded by amino acid residues 9-35 of SEQ ID NO: 4, a peptide encoded by amino acid residues 8-22 of SEQ ID NO: 4, or a peptide encoded by amino acid residues 71-84 of SEQ ID NO: 4 [p55a, p56a, p57a.].

55. (Amended) A method of producing a composition for treatment and/or prevention of pathoangiogenic conditions comprising:

providing at least one [GBS] Group B β-hemolytic *Streptococci* toxin receptor or immunogenic fragment thereof, and

formulating the receptor or fragment in a pharmaceutically acceptable excipient

whereby said composition is produced and

wherein the pathoangiogenic condition comprises cancer.

REMARKS

The present invention is related to methods and compositions for preventing or protecting against pathoangiogenic conditions by administering one or more Group B β-hemolytic *Streptococci* (GBS) toxin receptors or immunogenic fragments thereof to a mammal, in an amount sufficient to induce or maintain an immune response to at least one GBS toxin receptor. Claims 1, 3-16, 29-48, 55, and 56 are currently pending. Claims 1 and 3-16 are drawn to a method for preventing cancer in a mammal. Claims 30-48 are drawn to a composition for protecting against or attenuating cancer. Claims 55 and 56 are drawn to a method for producing a composition for treating and/or preventing cancer. In an effort to facilitate prosecution, Claims 1, 4-6, 8-12, 14-16, 29, 30, 32, 35, 37, 38, 40-42, 44-46, 48 and 55 have been amended herein and Claims 3 and 39 have been cancelled. No new matter is introduced by the amendments. Reexamination and reconsideration of the application are requested in view of these amendments and the remarks.

Election/Restriction

Applicant acknowledges entry of the Response to Restriction Requirement filed on June 21, 2002. Upon allowance of claims in the present application, applicant reserves the right to re-enter the subject matter of non-elected species.

Specification

In the October 21, 2002 Office Action, the Examiner noted that each letter of a trademark should be capitalized and demarcated with the appropriate symbol. The appropriate amendments have been entered herein and withdrawal of the rejection is therefore respectfully requested.

Claim Objections

Claims 1, 3-16, 29-48, 55 and 56 were objected to because they contained subject matter of non-elected inventions. In an effort to faciliatate prosecution, the relevant claims have been amended to remove the subject matter of non-elected inventions.

Claim 16 was objected to because the claim structure of the Markush group was improper. The appropriate amendment has been entered herein.

In light of the foregoing amendments, withdrawal of the objections is respectfully requested.

Claims Rejections – 35 U.S.C. § 112, first paragraph

Lack of Enablement

In the October 21, 2002 Office Action, the Examiner rejected Claims 1 and 3-16 under 35 U.S.C. §112, first paragraph for not being reasonably enabling for a method of preventing cancer in a mammal. The Examiner stated however, that the specification is enabling for a method for preventing melanoma in mice immunized with "HP59/CFA". Applicant respectfully submits that one skilled in the art would extrapolate the data provided in the specification showing the effectiveness of the invention for preventing melanoma in mice immunized with HP59/CFA to decreasing the incidence of cancer in mammals generally. Experimentation on mice and data generated therefrom is routinely extrapolated to the mammalian class generally, and also specifically for humans. Applicant respectfully provides therefore, that the present invention is enabled for preventing cancer in mammals. Applicant respectfully requests that the rejection be withdrawn.

In the October 21, 2002 Office Action, the Examiner rejected Claims 30-48 under 35 U.S.C. §112, first paragraph for not being reasonably enabling for a composition for protecting against or attenuating cancer. The Examiner stated however, that the specification is "enabling for a composition . . . for attenuating tumor burden in mice . . . and reasonably enabling for a method for protecting against the development of melanoma in mice." In an effort to facilitate prosecution, Applicant has herein amended claim 30 to more clearly state that the composition is for protecting against or attenuating cancer in mammals. As discussed above, experimental data generated using mice is routinely extrapolated to mammals in general. Accordingly, one skilled in the art would reasonably apply the teachings in the specification concerning mice, to mammals in general. Claims 31-48 depend from amended Claim 30 and contain all the

limitations thereof. Therefore, in view of the amendments, applicant respectfully requests that the rejection be withdrawn.

In the October 21, 2002 Office Action, the Examiner rejected Claims 55-56 under 35 U.S.C. §112, first paragraph for not being reasonably enabling for a method for producing a composition for treatment and/or prevention of cancer. The Examiner stated however, that the specification is "enabling for a method for producing a composition . . . for attenuating tumor burden in mice . . . and reasonably enabling for a method for producing a composition . . . for protecting against the development of melanoma in mice." In an effort to facilitate prosecution, Applicant has herein amended Claim 55 to more clearly state that the claimed methods are applicable to humans. The rationale for this amendment is provided in the two preceding paragraphs. Claim 56 depends from amended Claim 55 and contains all the limitations thereof. Therefore, in view of the amendments, applicant respectfully requests that the rejection be withdrawn.

Furthermore, page 5 of the Office Action acknowledges the data showing that mice immunized with compositions of the invention are smaller tumor burdens and survive longer than mice immunized with adjuvant and CFA. However, the Office Action states that the amount of exemplification provided in the specification is not reasonably commensurate in scope with claims to enable the skilled artisan to make and use the claimed invention with a reasonable expectation of success without having need to perform additional, undue experimentation.

Furthermore, page 6 of the Office Action states that the protection of patients against the development of cancer has proven intractable and a therapeutic benefit of administering cancer vaccines has been rarely observed For support the Office action cites research articles dated in the years 2000, 1994, and 1995. Applicant respectfully submits that vaccines for the treatment of cancer are currently considered to be highly promising by the medical community. Although the early stages of cancer vaccine development were faced with skeptism and challenge, more recent findings have reinstated confidence in the development of effective vaccines that can not only treat various manifestations of cancer, but also prevent them.

In support of applicant's position, please see Attachment A, *The Oncologist*, Vol.7, Suppl 3, 20-33, August 2002:

> "Only recently, major advances in cellular and molecular immunology have allowed a comprehensive understanding of the complex and high rate of interactions between the immune system and tumor cells...Substantial data from several preclinical models and early human clinical trails have confirmed the ability of cancer vaccines to induce immune responses that are tumor-specific and...associated with clinical responses." (Abstract)

As indicated in the preceding excerpt, the article discusses the efficacy of cancer vaccines and the steady development of improvements for such therapeutics. Applicant notes that the article is more recent than any of the references cited in the Office Action.

Claims Rejections – 35 U.S.C. § 112, first paragraph

Lack of Possession of the Claimed Invention

The Office Action rejects Claims 1, 3-16, 29-48, and 55-56 under 35 U.S.C. §112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention."

The Office Action states that the specification fails to describe a representative number of the members of the genus of GBS toxin receptors to which the claims refer. The Office Action notes that the specification only describes the receptors HP59 and SP55. In an effort to facilitate prosecution, applicant has herein amended the claims to recite the specific toxin receptors discussed in applicant's specification.

Claims Rejections – 35 U.S.C. § 112, second paragraph

Indefiniteness

The Office Action rejects Claims 1, and 3-16 under 35 U.S.C. §112, second paragraph, "because Claim 1 does not recite a positive process step that clearly relates back to the preamble of the claim." In an effort to facilitate prosecution, applicant has amended Claim 1 in accordance with the Examiner's recommendation. The Office Action rejects Claims 1, 3-16, 29-48, 55-56

under 35 U.S.C. §112, second paragraph, "because the claims use 'GBS' to designate 'Group B β-hemolytic *Streptococci*'." In an effort to facilitate prosecution, applicant has amended the relevant claims in accordance with the Examiner's recommendation.

The Office Action rejects Claims 2-14 and 40-48 under 35 U.S.C. §112, second paragraph, "because Claims 2-14 and 40-48 recite the term 'substantial'." The Office Action notes that "substantial" is a relative term and is not defined in the claims. Therefore, the Examiner believes that a skilled artisan would not be apprised of the metes and bounds of the invention. Applicant respectfully traverses.

On page 8 of applicant's specification, a detailed explanation of the meaning for the term "substantial identity" is provided. Applicant respectfully provides that one skilled in the art would reasonably appreciate the metes and bounds of the invention given the description provided in the specification.

The Office Action rejects Claims 7, 14, 44 and 48 under 35 U.S.C. §112, second paragraph, "because. . . the use of a laboratory designation only to identify a particular polypeptide renders the claim indefinite." In an effort to facilitate prosecution, applicant has amended the relevant claims in accordance with the Examiner's recommendation.

The Office Action rejects Claims 55 and 56 under 35 U.S.C. §112, second paragraph, "because Claim 55 does not recite a positive process step that clearly relates back to the preamble of the claim." In an effort to facilitate prosecution, applicant has amended the Claim 55 in accordance with the Examiner's recommendation.

Claims Rejections – 35 U.S.C. § 102

Anticipation

In the October 21, 2002 Office Action the Examiner rejected Claims 1, 3-7, 15, 16, 29-34, 37, 39-41, 43, 44, 55, and 56 under 35 U.S.C. §102 as being anticipated by Nair, *et al.* Nair, *et al.* teach a method for treating a mammal by immunizing the mammal with a composition containing antigen-presenting cells pulsed with tumor extracts. Applicant respectfully traverses.

The present invention is directed to a cancer vaccine that targets a unique protein that is expressed in mammals after a short period following birth, *but only* in mammals having a

pathoangiogenic condition. Specifically, the present invention is directed to a cancer vaccine that targets the Group B β-hemolytic *Streptococci* toxin receptors. In contrast. Nair *et al.* discuss a vaccine that results from the use of proteins or peptides encoded by antigens derived from tumor cells from patients. Unlike the present invention, variability of the targeted antigen is certainly an issue, "It is not known which of the currently known tumor-associated antigens will serve as effective antigens in a vaccine formulation." Nair et al. Gene Therapy 1998, vol 5 1445. Nair clearly fails to disclose a vaccine identical or even similar to the one claimed herein by the applicant. Indeed there is no mention of Group B β-hemolytic *Streptococci* toxin receptors at all. Applicant submits therefore, that the Nair *et al.* reference fails to anticipate the claimed invention.

No additional fees are believed due, however, the Commissioner is hereby authorized to charge any deficiencies which may be required or credit any overpayment to Deposit Account Number 11-0855.

In light of the above, Applicants respectfully submit that claims are allowable, and a Notice of Allowance is courteously solicited. The foregoing is submitted as a full and complete response to the Office Action mailed October 21, 2002 in United States Patent Application Serial No. 09/776,865. The Examiner is invited and encouraged to contact the undersigned attorney of record if such contact will facilitate an efficient examination and allowance of the application.

Respectfully submitted,

Sima Singadia Kulkarni
Reg. No. 43,732

KILPATRICK STOCKTON, LLP
Suite 2800
1100 Peachtree Street,
Atlanta, Georgia 30309–4530
(404) 815-6500
Our Docket: 22100-0100 (49530-252687)